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Mullan

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[54] NUCLEIC ACIDS FOR DIAGNOSING AND MODELING ALZHEIMER'S DISEASE

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[56] References Cited

U.S. PATENT DOCUMENTS

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|-----------|--------|--------------------|-----------|
| 4,912,206 | 3/1990 | Goldgaber et al. | 435/6 |
| 5,015,570 | 5/1991 | Scangos et al. | 536/24.31 |
| 5,218,100 | 6/1993 | Müller-Hill et al. | 536/23.5 |
| 5,220,013 | 6/1993 | Ponte et al. | 536/23.5 |
| 5,221,607 | 6/1993 | Cordell et al. | 536/23.5 |

FOREIGN PATENT DOCUMENTS

- 9207068 4/1992 WIPO .

OTHER PUBLICATIONS

Mullan et al., *Nat. Genet.* 1(5):345-347, (1992); abstracted in *Chem. Abst.* 117:607, Abst #148514a, (1992).
Kang et al., "The precursor of Alzheimer's disease amyloid

A4 . . ." *Nature* 325:733-736, (Feb. 1987).Yoshikai et al., "Genomic organization of the human amyloid . . . gene", *Gene* 87:257-263 (Mar. 1990).Murrell et al., "A Mutation in the Amyloid Precursor Protein . . ." *Science* 254:97-99.Chartier-Harlan et al., "Early-onset Alzheimer's disease caused by mutations at codon 717 of the β -amyloid precursor protein gene," *Nature* 353:844-847 (1991).Goate et al., "Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease," *Nature* 349:704-706 (1991).Levy et al., "Mutation of the Alzheimer's Disease Amyloid Gene in Hereditary Cerebral Hemorrhage, Dutch Type," *Science* 248:1124-1126 (1990).Primary Examiner—Stephen G. Walsh
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[57] ABSTRACT

The invention provides an isolated nucleic acid characteristic of human amyloid precursor protein 770 including the nucleotides encoding codon 670 and 671, wherein the nucleic acid encodes an amino acid other than lysine at codon 670 and/or an amino acid other than methionine at codon 671. Also provided is a method of diagnosing or predicting a predisposition to Alzheimer's disease, comprising detecting in a sample from a subject the presence of a mutation at a nucleotide position corresponding to codons 670 and/or 671 of amyloid precursor protein or fragment thereof, the presence of the mutation indicating the presence of or a predisposition to Alzheimer's disease.

12 Claims, 1 Drawing Sheet

